

What is claimed is:

- 1 A method for identifying a compound that induces a morphogen-mediated
2 biological effect, the method comprising the steps of:
- 3 (a) providing a test cell comprising DNA defining
4 a morphogen-responsive transcription activating element, and, in
5 operative association therewith, a reporter gene encoding a
6 detectable gene product,
7 said DNA, when present in a morphogen-responsive cell contacted with
8 morphogen, serving to induce transcription of said reporter gene;
- 9 (b) exposing said test cell to a candidate compound; and,
10 (c) detecting expression of said detectable gene product, said expression
11 indicating the ability of said candidate compound to induce said morphogen
12 mediated biological effect.
- 1 2. The method of claim 1 wherein said morphogen responsive transcription activating
2 element binds with a protein having general DNA-binding properties of a MEF-2
3 family protein, said DNA binding inducible by performing step (b).
- 1 3. The method of claim 1 wherein the nucleotide sequence of said morphogen
2 responsive transcription activating element comprises a sequence that hybridizes to
3 an MEF-2 binding site sequence.
- 1 4. The method of claim 1 wherein said morphogen responsive transcription activating
2 element comprises nucleotides 699-731 of Seq. ID No. 1.
- 1 5. The method of claim 1 wherein said morphogen responsive transcription activating
2 element comprises nucleotides 682-761 of Seq. ID No. 1.

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- 1 6. The method of claim 1 wherein said morphogen responsive transcription activating
2 element comprises a sequence of A and T residues.
- 1 7. The method of claim 6 wherein the sequence of A and T residues comprises
2 nucleotides 699-711 of Seq. ID No. 1.
- 1 8. The method of claim 6 wherein the sequence of A and T residues comprises
2 nucleotides 703-724 of Seq. ID No. 1.
- 1 9. The method of claim 6 wherein the A and T residues are adjacent to an AP-1
2 binding site sequence.
- 1 10. The method of claim 9 wherein the AP-1 binding site sequence comprises
2 nucleotides 715-724 of Seq. ID No. 1 or the nucleotide sequence depicted in Seq.
3 ID No. 2.
- 1 11. The method of claim 1 or 2 comprising the additional step of:
2 producing therapeutic-grade commercially-significant quantities of said
3 compound.
- 1 12. The method of claim 1 or 2 comprising the additional step of:
2 administering said compound to humans for therapeutic effect.
- 1 13. A method of producing a compound competent to induce a morphogen-mediated
2 biological effect, the method comprising the steps of:
3 (a) obtaining said compound by screening at least one candidate compound
4 according to the method of claim 1 or 2; and,
5 (b) producing said compound or a derivative thereof having substantially the
6 same ability as said compound to induce said morphogen mediated
7 biological effect.

1 14. The compound identified by the method of claim 1 or 2.

1 15. A method of assessing whether a sample comprises a substance competent to bind
2 to DNA, the sequence of which comprises nucleotides 699-731 of Seq. ID No. 1,
3 the method comprising the steps of:

4 (a) providing DNA, the sequence of which comprises nucleotides 699-731 of
5 Seq. ID No. 1;

6 (b) exposing said DNA to said sample; and,

7 (c) detecting the binding of said substance to said DNA.

1 16. A substance identified by the method of claim 15.

1 17. A substantially pure substance competent to bind to DNA, the sequence of which
2 comprises nucleotides 699-731 of Seq. ID No. 1, such that said substance has the
3 property of modulating expression of a gene encoding a gene product when said
4 DNA is in operative association therewith and said substance is bound thereto.

1 18. The substantially pure substance of claim 17 comprising a polypeptide, the amino
2 acid sequence of which comprises a sequence sharing homology with the
3 conserved domain of c-fos.

1 19. The substantially pure substance of claim 17 comprising a polypeptide having
2 general immunological properties of a c-fos family protein.

1 20. The substantially pure substance of claim 17 comprising a polypeptide comprising
2 an epitope bound by an antibody specific for a polypeptide immunogen having an
3 amino acid sequence comprising the sequence depicted in SEQ. ID No. 4.

1 21. The substantially pure substance of claim 17 comprising a polypeptide, the binding
2 of which to said DNA is inducible by a morphogen or analog thereof.

1 22. The substantially pure substance of claim 17 comprising a polypeptide having
2 general DNA-binding properties of a MEF-2 family protein.

1 23. The substantially pure substance of claim 21 or 22 wherein said substance is
2 competent to bind to DNA consisting of A and T residues.

1 24. An isolated DNA sequence defining a morphogen-responsive transcription
2 activating element comprising:

- 3 (a) nucleotides 699-731, 682-731, or 682-761 of SEQ. ID No. 1;
4 (b) species and allelic variants of (a);
5 (c) DNA which hybridizes to the strand complimentary to sequence (a)
6 and is morphogen-responsive under native conditions; and
7 (d) biosynthetic variants of any of (a), (b) and (c).

1 25. The isolated DNA sequence of claim 24 wherein said morphogen-
2 responsive transcription activating element comprises an MEF-2 binding
3 site sequence adjacent an AP-1 binding site sequence.

1 26. An isolated polypeptide chain comprising:

- 2 (a) a morphogen-inducible DNA binding protein which can interact
3 with nucleotides 699-711, 715-724, 699-731, 682-731, 703-724 or
4 682-761 of Seq. ID No. 1;
5 (b) species or allelic variants of (a);
6 (c) truncated amino acid sequences of any of (a) and (b) inducible by a
7 morphogen or analog thereof under native conditions;
8 (d) biosynthetic or recombinant variants of any of the above.

1 27. An isolated binding protein having binding specificity for a polypeptide
2 chain of claim 26. '

1 28. The isolated binding protein of claim 27 wherein said binding protein is an
2 antibody.

1 ~~29. A cell transfected with any one of the DNA sequences of claim 24 or 25.~~

1 30. A method of detecting a morphogen-mediated biological affect, the method
2 comprising the step of: detecting DNA binding of the protein of claim 26.

1 31. The method of claim 30 comprising the additional step of providing a
2 morphogen or a morphogen analog to a morphogen responsive cell prior to
3 said detecting step, and wherein said DNA binding is detected within about
4 2 to 12 hours.

1 32. The method of claim 30 comprising the additional step of providing a
2 morphogen or morphogen analog to a morphogen responsive cell prior to
3 said detecting step, and wherein said DNA binding is detected within about
4 2 to 6 hours.

1 33. ~~The method of claim 1, 2, 15 or 30 comprising part of a medium or high-~~
2 ~~flux screening assay.~~

1 34. ~~The method of claim 1 or 2 comprising the additional step of:~~
2 ~~producing therapeutic-grade commercially-significant quantities of~~
3 ~~said compound.~~

1 35. ~~The method of claim 1 or 2 comprising the additional step of:~~
2 ~~administering said compound to humans for therapeutic effect.~~

- 1 36. A method for identifying a candidate compound that induces a morphogen-
2 mediated biological effect, the method comprising the steps of:
3 (a) providing a test cell comprising DNA defining a morphogen
4 responsive transcription activating element, said DNA, when
5 present in a morphogen responsive cell contacted with morphogen,
6 serving to induce transcription of a reporter gene operatively
7 associated with said transcription activating element;
8 (b) exposing said test cell to a candidate compound; and
9 (c) detecting morphogen inducible DNA binding to said transcription
10 activating element by a cellular protein, said binding indicating the
11 ability of said candidate compound to induce said morphogen
12 mediated biological effect,
13 wherein step (c) occurs within approximately 2 - 12 hours of completing
14 step (b).
- 1 37. A method for monitoring cell differentiation or tissue morphogenesis
2 comprising the step of: detecting DNA binding of the protein of claim 21,
3 22, 23 or 26 in a cell exposed to a morphogen or analog thereof.
- 1 38. The method of claim 37 wherein said cell is a chondrocyte.
- 1 39. The method of claim 37 wherein said tissue is bone.
- 1 40. The method of claim 37 wherein said cell differentiation is chondroblast or
2 osteoblast cell differentiation.
- 1 41. The method of claim 37 wherein said DNA binding is detected within 2 to
2 6 hours of exposing said cell to said morphogen or analog thereof.

